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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

DREWE et al.

Serial No. 09/744,489

Filed: January 23, 2001

For: NUCLEIC ACID DETECTION BY  
TRIPLE HELIX FORMATION

Art Unit: 1637

Examiner: Suryaprabha Chunduru

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

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Commissioner for Patents  
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Sir:

Responsive to the Office Action dated May 5, 2006, ("Office Action"), the Final Office Action dated December 27, 2006 ("Final Office Action"), and the Advisory Action dated March 16, 2007 ("Advisory Action"), Applicants request a pre-appeal brief review in the application identified above. A concise statement setting forth the reasons for the request is set forth below.

## REASONS FOR THE REQUEST

In the Final Office Action and the Advisory Action, the Examiner has failed to establish a *prima facie* basis for rejecting Claims 1-2, 5-6, 8-9, 12 and 22-24 under 35 U.S.C. §103(a), as obvious over U.S. Patent No. 5,800,894 to Vary *et al.* ("Vary") in view of WO 96/02558 A1 to Egholm *et al.* ("Egholm"), and further in view of U.S. Patent No. 5,723,591 to Livak *et al.* ("Livak"). The Examiner has also failed to establish a *prima facie* basis for rejecting Claims 10-11 and 18-19 under 35 U.S.C. § 103(a), as obvious over Vary in view of Egholm and Livak, and further in view of WO 97/05280 to Graham *et al.*

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("Graham"). Finally, although Applicants believe that kit Claims 25 and 26 remain patentable over the cited combination of Graham and Egholm, Applicants would be willing to cancel these claims in order to expedite prosecution of the present application, without prejudice to their inclusion in a continuing application. These are the only remaining rejections in this case.

Applicants submit that Vary, Egholm, Livak and Graham fail to teach, suggest, or provide motivation to derive all elements of Applicants' claimed invention, and that they fail, separately or in combination, to render the claims *prima facie* obvious. Applicants respectfully request the review of the Examiner's erroneous rejections in view of the Remarks set forth below and in view of the previous arguments by Applicants.

#### REMARKS

The present application is directed to a method for detecting the presence of a target nucleic acid sequence in a sample by amplifying the target to produce an amplification reaction product that includes a purine rich region, contacting the sample during the amplification with a peptide nucleic acid able to bind to at least a portion of the target sequence and detecting the presence of triplex DNA structures. The application is also directed to a kit containing a bis-peptide nucleic acid (PNA) sequence designed to form a triplex with a target sequence and a set of amplification primers that can amplify a sequence including the target sequence.

Applicants traverse the rejection of Claims 1-2, 5-6, 8-9, 12 and 22-24 under 35 U.S.C. §103(a), as obvious over Vary in view of Egholm and Livak. Applicants assert that the Examiner has failed, as a matter of law, to establish a *prima facie* case of obviousness of these claims in view of the cited prior art. As set forth in the February 27, 2007 Amendment and Response to Office Action ("Amendment"), Vary discloses a method for detecting a nucleic acid target sequence by formation of a triplex structure, but fails to teach or suggest the use of a PNA probe to form this structure. Amendment, p. 6, ¶ 5. Egholm discloses novel PNAs such as bis-PNA, but fails to teach formation of a triplex structure during amplification. *Id.* at p. 7, ¶ 1. Livak discloses use of an oligonucleotide probe that includes a fluorescent reporter molecule and a quencher molecule—the quencher molecule is capable of quenching the fluorescence of the reporter for use in monitoring nucleic acid amplification. *Id.* at p. 8, ¶ 1.

In response to rejection of Claims 6 and 22-24 under 35 U.S.C. § 103(a) as obvious over Vary in view of Egholm, Applicants argued in the Amendment that Egholm teaches away from using PNA

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probes during an amplification reaction because Egholm teaches that PNA binds nucleic acid molecules with a high affinity, which should **impede amplification**. *Id.* at p. 7, ¶¶ 1-2. The Examiner found this argument persuasive, as explained in the Advisory Action in the "Continuation of 11" section, at ¶ 1.

With respect to the rejection of Claims 1-2, 5, 8-9, and 12 under 35 U.S.C. § 103(a) in view of the combination of Vary, Egholm and Livak, Applicants explained that one skilled in the art would have **avoided** the use of a PNA probe during amplification because, despite the known advantages of real-time PCR, in which an oligonucleotide probe is present during amplification, it would be **technically disadvantageous** to use a PNA probe during amplification of a target sequence due to the **high affinity of PNA for DNA**, as noted by Egholm. Amendment, at p. 8, ¶ 2. Applicants also cited to evidence published in the scientific literature **after** the present method was developed that has shown that nucleic acid amplification can be achieved in the presence of a complementary PNA. However, those skilled in the art found this result **surprising** in view of the known properties of PNA. *Id.* at ¶ 3.

The Examiner found these arguments unpersuasive, maintained the rejection of Claims 1-2, 5, 8-9, and 12, and applied the same arguments to reject Claims 6 and 22-24. Advisory Action, "Continuation of 11", ¶¶ 1-2. The Examiner explained that MPEP § 2112 provides that "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old **composition** patentably new to the discoverer." *Id.* at ¶ 2 (emphasis added, citations omitted).

**The Examiner's citation to MPEP § 2112 in this instance is incorrect as a matter of law.** The authority to which the Examiner cites relates to the general proposition that discovery of new properties of a known **composition** that were inherent, but unappreciated, in the composition are not patentable. Independent Claims 1 and 6 of the present application, however, to which these arguments are applied, are **process claims**. As explained in great detail by the Federal Circuit in *Catalina Marketing International, Inc. v. Coolsavings.com, Inc.*, it is axiomatic that **new uses for known compositions are patentable**. 289 F.3d 801, 810 (Fed. Cir. 2002) ("The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." (quoting 35 U.S.C. § 100(b))). Accordingly, the Examiner has failed to rebut Applicants' arguments that it would be technically disadvantageous to use a PNA probe during amplification of a target sequence due to the high affinity of PNA for DNA.

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Moreover, the Examiner characterizes the Applicants' arguments that one skilled in the art would have avoided using a PNA probe during amplification as "contradictory because inspite [sic] of its disadvantages the instant invention uses a PNA probe during amplification." Applicants disagree. Applicants have discovered and claimed novel methods for detecting the presence of a target nucleic acid sequence in a sample. This novel discovery cannot be used as evidence against the present claims—the Examiner must instead point to evidence in the prior art to rebut Applicants' arguments. The Examiner's circular logic of applying Applicants' own claims as evidencing the skill in the art is the use of impermissible hindsight in its purest form, and is incorrect as a matter of law. *See generally* MPEP §§ 2143 and 2145. Moreover, "[t]he totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. . . . Furthermore, known disadvantages in old devices which would naturally discourage search for new inventions may be taken into account in determining obviousness." MPEP § 2145 (citations and internal quotations omitted).

With respect to the rejection of Claims 10-11 and 18-19 under 35 U.S.C. § 103(a) as obvious over Vary in view of Egholm and Livak, and further in view of Graham, Applicants submit that, for the reasons discussed above, the Vary, Egholm and Livak combination fails to establish a *prima facie* case of obviousness of these claims. Moreover, Graham fails to cure the deficiencies of Vary, Egholm and Livak. Accordingly, Applicants submit that Claims 10-11 and 18-19 are novel and nonobvious over the combination of references cited by the Examiner.

Applicants believe Claims 25 and 26 to be patentable over the combination of Graham and Egholm. However, in order to expedite prosecution of the present application, Applicants would be willing to cancel these claims, without prejudice to their inclusion in a continuing application.

In view of the foregoing, Applicants submit that Vary, Egholm, Livak and Graham fail to teach, suggest, or provide motivation to derive all elements of the presently claimed invention, and therefore they fail, separately or in combination, to render the claims *prima facie* obvious. Applicants accordingly respectfully request withdrawal of the rejection of Claims 1-2, 5-6, 8-12, 18-19 and 22-26 under 35 U.S.C. §103(a).

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### CONCLUSION

For the reasons set forth above, Applicants respectfully request that the pending claims be allowed.

Respectfully submitted,



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